Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Previously presented) A method of performing targeted modifications of human embryonic stem (ES) cells, the method comprising the steps of

obtaining copies of a genetic construct, wherein the construct is a targeting vector comprising 5' and 3' arms flanking an insert that is homologous to a genomic region flanking a site in the genome of the ES cells selected for insertion, so that homologous recombination will occur between the genetic construct and the selected regions of the stem cell genome;

electroporating the copies of the genetic construct into human ES cells in culture; and

identifying cells which contain the genetic construct, wherein the construct includes a marker gene for cellular identification.

2. (Cancelled)

3. (Previously presented) A method as claimed in claim 1 wherein there is no promoter on the marker gene in the genetic construct, the genetic construct being inserted into the ES cells in a location in the genome of the ES cells wherein the marker gene is expressed only in cells in a desired state of differentiation.

4. (Previously presented) A method as claimed in claim 1 wherein the vector includes a tissue specific promoter driving the expression of the marker gene in the genetic construct, the tissue specific promoter being active only in cells in a desired state of differentiation.

5. (Withdrawn) Human cells in culture derived from human embryonic stem cells, the cells comprising in their genome an inserted genetic construct which knocks out the functioning of a gene which would otherwise be expressed in those human cells in culture.

6. (Withdrawn) Human cells in culture derived from human embryonic stem cells, the cells comprising in their genome an inserted genetic construct which introduced a mutation into a native gene in those human cells in culture.

7. (Previously presented) A method of purifying cells of a defined lineage from a culture of human embryonic stem (ES) cells, the method comprising the steps of

(a) obtaining copies of a genetic construct, wherein the construct is a targeting vector comprising 5' and 3' arms flanking an insert that is homologous to a genomic region flanking a site in the genome of the ES cells selected for insertion, so that homologous recombination will occur between the genetic construct and the selected regions of the genome of the stem cells, the genetic construct including a marker gene for cellular identification which will be expressed only in cells of the defined lineage;

(b) electroporating the copies of the genetic construct into human ES cells in culture;

(c) identifying cells which express the marker gene from the genetic construct; and

(d) purifying the cells expressing the marker from cells not expressing the marker.

8. (Previously presented) A method as claimed in claim 7 wherein the marker gene includes a promoter which is active to express a gene only in cells of the defined lineage.

9. (Original) A method as claimed in claim 7 wherein after the electroporating step, the ES cells are permitted to differentiate.

10. (Previously presented) A method as claimed in claim 7 wherein the marker gene encodes a fluorescent gene product and the identifying and purifying is performed by fluorescence activated cell sorting.

11. (Withdrawn) A culture of differentiated human cells derived from human ES cells and purified by the method of claim 7 for cells of a desired lineage.

12. (Previously presented) A method for purifying cells of a defined lineage obtained from human embryonic stem (ES) cells, the method comprising the steps of

a) analyzing the gene expression pattern of the cells with the defined lineage purified by the method of Claim 7 to identify genes expressed in the cells of the defined lineage which are characteristic of that lineage;

b) culturing non-transformed human ES cells in the presence of genes characteristic of a defined lineage identified in step a) and under conditions capable of differentiating the ES cells into cells of the defined lineage; and

c) purifying the cells of step b) that are of the defined lineage based upon the expression of the genes identified in the analyzing step.

13. (Original) A method as claimed in claim 12 wherein the defined lineage is undifferentiated cells wherein the genes identified include genes for the cellular factors CD124, CD113, FGF-R, c-Kit, and BMP-4, and wherein the purification step is performed by testing cells for expression of at least one gene selected from the groups consisting of CD124, CD113, FGF-R, c-Kit, and BMP-4.

14. (Withdrawn) Human cells in culture derived from human embryonic stem cells, the cells comprising in their genome an inserted genetic construct which expresses an inserted gene only when the human cells are in a desired state of differentiation.

15. (Withdrawn) Human cells in culture as claimed in claim 14 wherein the desired state of differentiation is an undifferentiated state.

16. (Withdrawn) Human cells in culture as claimed in claim 14 where the gene is a marker gene the expression of which can be observed visually.

17. (Previously presented) A method of performing targeted modifications of human embryonic stem (ES) cells, the method comprising the steps of

a) electroporating copies of a genetic construct into human ES cells in culture, wherein the construct is a targeting vector comprising a foreign gene and a marker gene flanked by 3' and 5' arms homologous to a genomic region flanking a site in the genome of the ES cells selected for insertion, so that homologous recombination will occur between the genetic construct and the selected regions of the stem cell genome,

(i) wherein the marker gene comprises a promoter active in cells of a defined lineage, or

(ii) wherein in the absence of a promoter, the construct is designed to recombine with the selected regions of the ES cell genome, such that the marker gene is operably linked to an endogenous, tissue specific promoter; and

b) identifying cells which express the marker gene from the genetic construct.

18. (Previously presented)The method of claim 17, further comprising purifying the cells of step b) expressing the marker from cells not expressing the marker, wherein the cells expressing the marker are of a defined lineage.